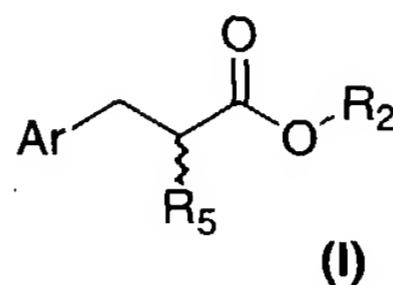


What is claimed:

1. A method of resolving a racemic mixture of a compound of formula I to obtain a desired enantiomer:

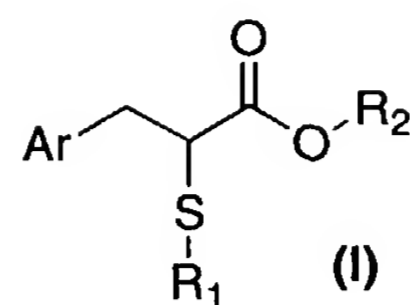


wherein Ar is C<sub>6</sub> or C<sub>10</sub> aromatic group that can be substituted with H, C<sub>1</sub> to C<sub>6</sub> alkyl, trifluoromethyl or halo, R<sub>5</sub> is halo or -S-R<sub>1</sub>, wherein R<sub>1</sub> is H or acetyl, and R<sub>2</sub> is H or C<sub>1</sub> to C<sub>6</sub> alkyl, the method comprising:

reacting a compound of formula I wherein the compound is an ester whereby R<sub>2</sub> is C<sub>1</sub> to C<sub>6</sub> alkyl with a lipase derived from *Mucor meihei* to stereoselectively hydrolyze the ester bond to produce an acid; and isolating the acid,

wherein the reaction is conducted in a solvent comprising 80% to 98% v/v% organic phase and a residue of water phase (which can be buffered).

2. The method of claim 1, wherein the solvent is selected to be effective to (a) produce an enantiomeric excess of the desired enantiomer of the acid of at least 88% and (b) preserve at least 90% of the enzymatic activity of the lipase.
3. The method of claim 1, wherein the lipase is immobilized on particles of a solid support.
4. The method of claim 1, wherein the organic component of the solvent comprises at least 80% t-butanol, acetonitrile or acetone.
5. The method of claim 1, wherein R<sub>1</sub> is acetyl.
6. A method of stereoselectively producing a desired enantiomer of a compound of formula I:

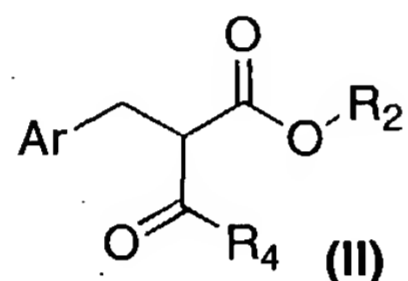


wherein Ar is C<sub>6</sub> or C<sub>10</sub> aromatic group that can be substituted with H, C<sub>1</sub> to C<sub>6</sub> alkyl, trifluoromethyl or halo, R<sub>1</sub> is H or acetyl, and R<sub>2</sub> is H or C<sub>1</sub> to C<sub>6</sub> alkyl, the method comprising:

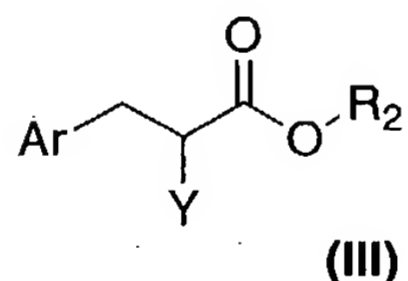
reacting Ar-CH<sub>2</sub>-X, where X is a leaving group, with

R<sub>4</sub>-C(O)-CH<sub>2</sub>-C(O)O-R<sub>2</sub>\*, wherein R<sub>2</sub>\* and R<sub>4</sub> are independently C<sub>1</sub> to C<sub>6</sub> alkyl;

reacting a resulting compound of formula II:

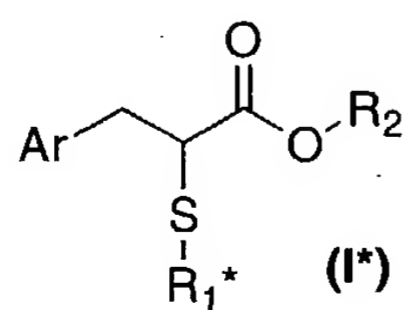


with a halogenating agent which comprises an N-halo substituted amide, N-halosubstituted imide, N-halosubstituted thioamide, or N-halosubstituted thioimide as the halogenating moiety to produce, with or without an additional hydrolysis of the ester, a compound of formula III:



wherein Y is the leaving group;

reacting the compound of formula III with Z-S-R<sub>1</sub>\*, wherein R<sub>1</sub>\* is acetyl, and Z is K, Na, or other cation to produce a compound of formula I\*: and



conducting one of the following stereoselective reactions:

(a)

- (1) reacting the compound of formula III with a hydrolase that is stereoselective for the ester;
- (2) isolating the desired resulting acid;
- (3) racemizing residual compound of formula III; and
- (4) conducting at least one additional iteration of steps (a)(1) and (a)(2) with the racemized residual compound of formula III, wherein the reacting with Z-S-R<sub>1</sub>\* is conducted with stereoselective inversion of the chiral carbon; or

(b)

- (1) reacting the compound of formula I\* with a hydrolase that is stereoselective for the ester;
- (2) isolating the desired resulting acid;
- (3) racemizing residual compound of formula I\*; and
- (4) conducting at least one additional iteration of steps b(1) and b(2) with the residual racemized compound of formula I\*.

7. The method of claim 6, further comprising: crystallizing the compound of formula I\* to obtain the compound of formula I\* in increased enantiomeric purity.

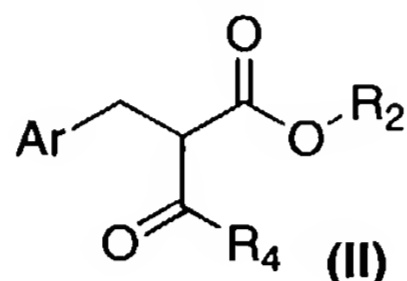
8. The method of claim 7, wherein the isomeric purity of the compound of formula I\* is at least 98%ee.

9. The method of claim 6, wherein the racemization steps of a(3) and b(3) comprises reacting with a catalytic amount of tetraalkylammonium halide.

10. The method of claim 6, wherein the halogenating agent is N,N-dibromo-5,5-dimethylhydantoin.

11. The method of claim 6, wherein the halogenating agent is N,N-dichloro-5,5-dimethylhydantoin.

12. A method of preparing a compound of formula II:



wherein  $R_2$  and  $R_4$  are independently  $C_1$  to  $C_6$  alkyl, the method comprising: reacting at least five equivalents of  $R_4-C(O)-CH_2-C(O)O-R_2$  with  $ArCH_2Cl$  wherein  $Ar$  is  $C_6$  or  $C_{10}$  aromatic group that can be substituted with  $C_1$  to  $C_6$  alkyl or halo, wherein the reaction is conducted in a solution consisting essentially of the reactants and no more than 1.2 molar equivalents of a base source of sodium, potassium, or lithium  $C_2$  to  $C_6$  alkoxide, which can be provided in the corresponding alcohol.

13. The method of claim 12, wherein the alkoxide concentration in the base source is at least 3 M.